

A Word of Caution in Considering the Use of the Lipoarabinomannan Lateral Flow Assay on Cerebrospinal Fluid for Detection of Tuberculous Meningitis

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We read with great interest the recent article by Cox et al. regarding the use of the lipoarabinomannan (LAM) lateral flow assay (Determine TB LAM; Alere, Waltham, MA, USA) on cerebrospinal fluid (CSF) for postmortem diagnosis of tuberculous meningitis (TBM) (1). Certainly, TBM is difficult to diagnose, and a delay in diagnosis often leads to poor outcomes for patients with TBM, including death (2, 3). Despite the recent interest in the use of Xpert MTB/Rif for TBM diagnosis (4–6), its sensitivity and negative predictive value remain insufficient for the use of Xpert as a “rule-out” test. The lack of sufficiently accurate and rapid diagnostics for TBM makes LAM an attractive candidate for TBM diagnosis.

Cox and colleagues obtained CSF from the fourth ventricle of 91 subjects at autopsy (1). Samples were stored at -20°C initially, later thawed, and then heated to 95 to 100°C . After cooling, the samples were further processed by spinning (1 ml) at 10,000 rpm for 15 min. LAM testing was performed with 60 μl of the supernatant, as well as unprepared CSF (aside from having been frozen) (1). When examining LAM with unprepared CSF against histopathologically definite or probable TBM, the authors found 50% sensitivity and 70% specificity. Against definite TBM cases, 75% sensitivity and 70% specificity were observed (1). When treated CSF supernatant was used, the authors found 88% sensitivity and 70% specificity of LAM against definite TBM cases and 71% sensitivity and 70% specificity against definite or probable cases.

These results, if clinically applicable, would rival any currently available technology (4–6). Importantly, this study used autopsy specimens rather than diagnosing living persons via CSF obtained by lumbar puncture. Obtaining CSF from the fourth ventricle, while possible, is much more invasive and is not frequently performed in most settings.

As part of our recent evaluation of the role of centrifugation of CSF specimens prior to testing for TBM using Xpert MTB/Rif, we evaluated the TB LAM lateral flow assay used in the study by Cox

and colleagues (6). In our use of the TB LAM lateral flow assay, we did not centrifuge the samples. We did use the same volume of CSF (60 μl) that Cox and colleagues used to test unprepared CSF. We tested CSF directly after lumbar puncture without freezing samples. Unfortunately, the sensitivity of this assay was far inferior to that reported by Cox and colleagues when the assay was used with CSF obtained via lumbar puncture from persons with meningitis. Of 67 samples tested by TB LAM, 0 reacted positively (6). Of those tested, 12 had definite TBM as diagnosed by positive Xpert MTB/Rif and/or culture (6). Two additional cases that tested negative by LAM had probable TBM, as determined by consensus research case definitions (6, 7).

Thus, while the study by Cox et al. makes one wonder whether or not the LAM lateral flow assay might be of use in TBM diagnosis, our experience was that this assay was very insensitive when used to attempt diagnosis of TBM in real time by using CSF obtained via lumbar puncture. The study by Cox and colleagues might support the use of LAM as a research tool in postmortem studies but not as an antemortem diagnostic test. Clearly, more data are needed to draw firm conclusions; however, we advocate caution in considering the use of the TB LAM lateral flow assay for the diagnosis of TBM.

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